Health Canada Santé Canada

Your health and safety... our priority. *Votre santé et votre sécurité... notre priorité.*

Proposed Registration Decision PRD2011-13

Metarhizium anisopliae strain F52

(publié aussi en français)

09 September 2011

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

Publications
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6604-E2
Ottawa, Ontario
K1A 0K9

Internet: pmra.publications@hc-sc.gc.ca
healthcanada.gc.ca/pmra
Facsimile: 613-736-3758
Information Service:
1-800-267-6315 or 613-736-3799
pmra.infoserv@hc-sc.gc.ca

Canada

ISSN: 1925-0878 (print)
1925-0886 (online)

Catalogue number: H113-9/2011-13E (print version)
H113-9/2011-13E-PDF (PDF version)

© Her Majesty the Queen in Right of Canada, represented by the Minister of Health Canada, 2011

All rights reserved. No part of this information (publication or product) may be reproduced or transmitted in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, or stored in a retrieval system, without prior written permission of the Minister of Public Works and Government Services Canada, Ottawa, Ontario K1A 0S5.

Table of Contents

Overview 1
Proposed Registration Decision for *Metarhizium anisopliae* strain F52 1
What Does Health Canada Consider When Making a Registration Decision? 1
What Is *Metarhizium anisopliae* strain F52? 2
Health Considerations 2
Environmental Considerations 4
Value Considerations 4
Measures to Minimize Risk 4
Next Steps 5
Other Information 5
Science Evaluation 7
1.0 The Active Ingredient, Its Properties and Uses 7
2.0 Methods of Analysis 7
2.1 Methods to Show Absence of Any Human and Mammalian Pathogens 7
2.2 Methods to Determine Storage Stability, Shelf-life of the Microorganism 7
3.0 Impact on Human and Animal Health 7
3.1 Toxicology Summary 8
4.0 Impact on the Environment 8
5.0 Value 8
6.0 Pest Control Product Policy Considerations 8
7.0 Summary 8
7.1 Methods for Analysis of the Micro-organism as Manufactured 8
7.2 Human Health and Safety 9
7.3 Environmental Risk 9
7.4 Value 9
7.5 Unsupported Uses 9
8.0 Proposed Regulatory Decision 9
List of Abbreviations 11
Appendix I Tables and Figures 13
Table 1 Toxicity of Met52 Granular Bioinsecticide 13
References 15

Overview

Proposed Registration Decision for *Metarhizium anisopliae* strain F52

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of *Metarhizium anisopliae* strain F52 and the end-use product Met52 Granular Bioinsecticide, containing the technical grade active ingredient *Metarhizium anisopliae* strain F52, to control root weevils, specifically black vine weevil and strawberry root weevil, on container-grown ornamentals.

Metarhizium anisopliae strain F52 (Registration Number 29146) and Met52 Granular Bioinsecticide (Registration Number 29147) are conditionally registered in Canada. The detailed review for *Metarhizium anisopliae* strain F52 and Met52 Granular Bioinsecticide can be found in Evaluation Report ERC2010-01: *Metarhizium anisopliae* strain F52. The current applications were submitted to convert *Metarhizium anisopliae* strain F52 and Met52 Granular Bioinsecticide from conditional registration to full registration.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

This Overview describes the key points of the evaluation, while the Science Evaluation section provides detailed technical information on the human health, environmental and value assessments of *Metarhizium anisopliae* strain F52 and Met52 Granular Bioinsecticide.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

---

1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact."

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (e.g. children) as well as organisms in the environment (e.g. those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the PMRA's website at healthcanada.gc.ca/pmra.

Before making a final registration decision on *Metarhizium anisopliae* strain F52, the PMRA will consider all comments received from the public in response to this consultation document[3]. The PMRA will then publish a Registration Decision[4] on *Metarhizium anisopliae* strain F52, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation of this consultation document.

What Is *Metarhizium anisopliae* strain F52?

Metarhizium anisopliae strain F52 is a soil-dwelling fungus that causes a fatal disease in certain insects. Formulated as Met52 Granular Bioinsecticide and incorporated into the growing medium, it can provide control of root weevils, specifically black vine weevil and strawberry root weevil, on container-grown ornamentals.

Health Considerations

Can Approved Uses of *Metarhizium anisopliae* strain F52 Affect Human Health?

***Metarhizium anisopliae* strain F52 is unlikely to affect your health when Met52 Granular Bioinsecticide is used according to the label directions.**

People could be exposed to *Metarhizium anisopliae* strain F52 when handling and applying the product. When assessing health risks, several key factors are considered: the microorganism's biological properties (e.g., production of toxic by-products), reports of any adverse incidents, its potential to cause disease or toxicity as determined in toxicological studies and the level to which people may be exposed relative to exposures already encountered in nature to other isolates of this microorganism.

---

3 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

4 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Toxicological studies in laboratory animals describe potential health effects from large doses in order to identify any potential pathogenicity, infectivity and toxicity concerns. When spores of *Metarhizium anisopliae* strain F52 and Met52 Granular Bioinsecticide were tested on laboratory animals, no signs of significant toxicity or disease were observed.

Residues in Water and Food

Dietary risks from food and water are not of concern.

The *Food and Drugs Act* prohibits the sale of food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value determines the maximum concentration in parts per million of a pesticide allowed in or on certain foods. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

As there are no direct applications to food and as no adverse effects were reported in laboratory studies, the establishment of an MRL is not required for *Metarhizium anisopliae* strain F52 under Section 4(d) of the *Food and Drugs Act* (adulteration of food) as defined under Division 15, Section B.15.002 of the Food and Drugs Regulations. In addition, the likelihood of residues of *Metarhizium anisopliae* strain F52 contaminating drinking water supplies is negligible. Consequently, dietary exposure and risk are minimal to non-existent.

Occupational Risks From Handling Met52 Granular Bioinsecticide

Occupational risks are not of concern when Met52 Granular Bioinsecticide is used according to label directions, which include protective measures.

Workers using Met52 Granular Bioinsecticide can come into direct contact with *Metarhizium anisopliae* strain F52 on the skin, in the eyes, or by inhalation. For this reason, the label will specify that users exposed to Met52 Granular Bioinsecticide must wear waterproof gloves, eye goggles, a long-sleeved shirt, long pants, shoes plus socks and a dust/mist filtering respirator/mask (MSH/NIOSH approval number prefix TC-21C) or a NIOSH-approved respirator/mask with any N-95, R-95, P-95 or HE filter.

For bystanders, exposure is expected to be much less than that of handlers and mixer/loaders and is considered negligible. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When Met52 Granular Bioinsecticide Is Introduced Into the Environment?

Environmental risks are not of concern.

Metarhizium anisopliae strain F52 is a non-indigenous soil microorganism that is pathogenic to specific host insects. Since the reproduction of conidiospores is reliant upon infection of a suitable host under conditions of high humidity, the proliferation of *Metarhizium anisopliae* strain F52 in the environment would be limited. It is likely that levels of *Metarhizium anisopliae* strain F52 would return to levels comparable to native populations of *Metarhizium anisopliae*.

Toxicity testing on non-target organisms shows that *Metarhizium anisopliae* strain F52 is capable of causing some adverse effects to certain aquatic organisms when exposed to high concentrations. However, the incorporation of Met52 Granular Bioinsecticide into the growing medium of potted plants is unlikely to result in significant contamination of aquatic environments. Therefore, the risk to aquatic organisms from the use of Met52 Granular Bioinsecticide is very low. Toxicity testing also shows that terrestrial non-target organisms, other than target insect species, were not adversely affected by *Metarhizium anisopliae* strain F52 when exposed to high concentrations.

Value Considerations

What Is the Value of Met52 Granular Bioinsecticide?

Incorporated into the growing medium, Met52 Granular Bioinsecticide can provide control of black vine weevil and strawberry root weevil on container-grown ornamentals.

The value of Met52 Granular Bioinsecticide is that it provides a viable alternative for the control of certain serious pests on a variety of crops. Root weevils, particularly black vine weevil and strawberry root weevil, are major pests of many ornamentals and are considered very difficult to control. Few other pest control products are registered in Canada for use against these pests and most are older, conventional chemical insecticides. Met52 Granular Bioinsecticide must be incorporated into the growing medium to achieve acceptable efficacy, but also may remain viable for nine months after application.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures on the label of Met52 Granular Bioinsecticide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Due to concerns about users developing allergic reactions through repeated high exposure to *Metarhizium anisopliae* strain F52, anyone handling or applying Met52 Granular Bioinsecticide must wear waterproof gloves, eye goggles, a long-sleeved shirt, long pants, shoes plus socks and a dust/mist filtering respirator/mask (MSH/NIOSH approval number prefix TC-21C) or a NIOSH-approved respirator/mask with any N-95, R-95, P-95 or HE filter.

Environment

As a general precaution, statements have been added to the label to prohibit handlers from contaminating aquatic habitats or allowing effluent from greenhouses containing this product to enter lakes, streams, ponds or other water bodies.

Next Steps

Before making a final registration decision on *Metarhizium anisopliae* strain F52, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments.

Other Information

When the PMRA makes its registration decision, it will publish a Registration Decision on *Metarhizium anisopliae* strain F52 (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

Metarhizium anisopliae strain F52

1.0 The Active Ingredient, Its Properties and Uses

For the identity of the active ingredient, physical and chemical properties of the active ingredient and end-use product, as well as the directions for use and mode of action pertaining to *Metarhizium anisopliae* strain F52 and Met52 Granular Bioinsecticide, please refer to Evaluation Report ERC2010-01: *Metarhizium anisopliae* strain F52.

2.0 Methods of Analysis

For a comprehensive review of the method[illegible]analysis pertaining to *Metarhizium anisopliae* strain F52 and Met52 Granular Bioinsecticide, please refer to ERC2010-01.

2.1 Methods to Show Absence of Any Human and Mammalian Pathogens

Confirmatory microbial contamination analysis data on five full scale production batches of the technical grade active ingredient, *Metarhizium anisopliae* strain F52, and end-use product, Met52 Granular Bioinsecticide, were required as a condition of registration.

Data were submitted by the registrant and the products were shown to be within acceptable microbial contamination limits established by the PMRA.

2.2 Methods to Determine Storage Stability, Shelf-life of the Microorganism

A storage stability study conducted with the end-use product confirming the acceptability of the stated storage period and conditions was required as a condition of registration.

The viability of *Metarhizium anisopliae* strain F52 in the end-use product, Met52 Granular Bioinsecticide, and technical grade active ingredient, *Metarhizium anisopliae* strain F52, was assessed over a range of time and storage temperatures. The submitted storage stability study supports a storage period of 12 months when Met52 Granular Bioinsecticide and *Metarhizium anisopliae* strain F52 are stored at or below 23°C.

3.0 Impact on Human and Animal Health

For details on the comprehensive toxicology review and human health risk assessment for *Metarhizium anisopliae* strain F52 and Met52 Granular Bioinsecticide, please refer to ERC2010-01.

3.1 Toxicology Summary

An acute toxicity study was required as a condition of registration to ensure that Met52 Granular Bioinsecticide is toxicologically equivalent to the technical grade active ingredient for which a full toxicological data package was submitted and determined to be acceptable.

In an acute oral toxicity study, one group of ten (five female; five male) fasted, nine week old albino Sprague-Dawley rats were given a single oral dose of Met52 Granular Bioinsecticide (1.85×10^9 viable spores/g) mixed with deionized water at 40% w/v at doses of 2020 mg/kg bodyweight. The animals were then observed for a period of up to 14 days. Controls groups were not employed. There were no treatment related clinical signs or necropsy findings. There was no effect on body weight gain with the exception of weight loss in one female during the second week. This study is classified as acceptable and satisfies the guideline requirement for an acute oral toxicity study in the rat for the end-use product. Based on the results of this study, Met52 Granular Bioinsecticide is of low toxicity, and toxicologically equivalent to the technical grade active ingredient.

4.0 Impact on the Environment

For a comprehensive review of the impact of *Metarhizium anisopliae* strain F52 and Met52 Granular Bioinsecticide on the environment, please refer to ERC2010-01.

5.0 Value

For a comprehensive review of the value of Met52 Granular Bioinsecticide, please refer to ERC2010-01.

6.0 Pest Control Product Policy Considerations

For a comprehensive review of the Toxic Substances Management Policy considerations and formulants and contaminants of health of environmental concern pertaining to *Metarhizium anisopliae* strain F52 and Met52 Granular Bioinsecticide, please refer to ERC2010-01.

7.0 Summary

7.1 Methods for Analysis of the Micro-organism as Manufactured

The confirmatory microbial contamination data were found to meet the specified contamination limits.

The submitted storage stability study supports a storage period of 12 months when Met52 Granular Bioinsecticide and *Metarhizium anisopliae* strain F52 are stored at or below 23°C.

These data satisfy the conditions of registration.

7.2 Human Health and Safety

The acute oral toxicity study submitted successfully showed that the end-use product is of low toxicity and, therefore, toxicologically equivalent to the technical grade active ingredient which satisfactorily addresses the condition of registration.

7.3 Environmental Risk

The non-target studies, scientific rationales and published scientific literature submitted in support of *Metarhizium anisopliae* strain F52 were determined to be sufficiently complete to permit a decision on registration. For a comprehensive review of the impact of *Metarhizium anisopliae* strain F52 and Met52 Granular Bioinsecticide on the environment, please refer to ERC2010-01.

As a precaution, standard label statements prohibit handlers from contaminating aquatic habitats or allowing effluent from greenhouses containing this product to enter lakes, streams, ponds or other water bodies.

7.4 Value

Met52 Granular Bioinsecticide has value for control of all growth stages of root weevils, specifically black vine weevil and strawberry root weevil, when incorporated into the growing medium of container-grown ornamentals. For a comprehensive review of the value of Met52 Granular Bioinsecticide, please refer to ERC2010-01.

7.5 Unsupported Uses

Acceptable efficacy has not been demonstrated when Met52 Granular Bioinsecticide is applied as a top dressing or to the soil in established field crops. For a comprehensive review of the value of Met52 Granular Bioinsecticide, please refer to ERC2010-01.

8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of *Metarhizium anisopliae* strain F52 and the end-use product Met52 Granular Bioinsecticide, containing the technical grade active ingredient *Metarhizium anisopliae* strain F52, to control root weevils, specifically black vine weevil and strawberry root weevil, on container-grown ornamentals.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

List of Abbreviations

°C	degree(s) Celsius
bw	body weight
g	gram(s)
HE	high efficiency
kg	kilogram(s)
LD_{50}	lethal dose 50%
mg	milligram(s)
MRL	maximum residue limit
MSH	Mine Safety and Health Administration
NIOSH	National Institute for Occupational Safety and Health
PMRA	Pest Management Regulatory Agency
w/v	weight per volume

Appendix I Tables and Figures

Table 1 Toxicity of Met52 Granular Bioinsecticide

Study Type	Species, Strain, and Doses	Results	Significant Effects and Comments	Reference
Acute Toxicity Met52 Granular Bioinsecticide				
Acute Oral Toxicity	Rat – Sprague Dawley 5/sex/dosed with Met52 Granular Bioinsecticide (1.85 × 10^9 viable spores/g) at 2020 mg/kg bw. No control group Bodyweight measured on days 0, 7, and 14.	14-day oral LD_{50} > 2020 mg/kg bw (male, female)	-no mortalities, no treatment related clinical signs, no necropsy findings, weight loss in one female during the second week LOW TOXICITY	1931317

References

A. List of Studies/Information Submitted by Registrant

1931304 Analysis for Microbial Contaminants: Metarhizium anisopliae strain F52 (#29146), DACO: M2.10.2 CBI

1931315 Analysis for Micorbial Contaminants: Met52 Granular Bioinsecticide (#29147), DACO: M2.10.2 CBI

1931316 Stability Study: Met52 Granular Bioinsecticide (#29147), DACO: M2.11

1931317 Met52 Granular Bioinsecticide: Acute Oral Toxicity Study in Rats, DACO: M4.2.2